

## **Non-technical Abstract**

We are studying the possibility of slowing the growth of ovarian cancer with a new method, gene therapy. Gene therapy replaces a defective or malfunctioning gene responsible for development of the cancer. In this study we will use a gene responsible for both hereditary and sporadic ovarian cancer, BRCA1. Research has shown that both inherited and non-inherited forms of ovarian cancer have defects in the BRCA1 gene and that gene transfer into ovarian cancer cells inhibits tumor growth. By introducing the normal BRCA1 gene into ovarian cancer cells which contain a defective BRCA1 gene, we hope to stop tumor growth by correcting the gene defect. The purpose of this study is to use a retrovirus to deliver the full length BRCA1 gene to the ovarian cancer cells and evaluate the effect on tumor growth in patients.

Initial preclinical experiments in mice have shown that gene transfer of the BRCA1 gene into ovarian cancer results in a marked decrease in the growth or spread of cancer. We have completed a phase I study using BRCA1 gene replacement in 12 patients with ovarian cancer. The results from this study demonstrated that this therapy produced minimal side effects (far less than standard chemotherapy) and was associated with a reduction of tumor in some patients. Based on these findings, we performed a partial phase II human clinical trial to further investigate the potential efficacy of BRCA1 gene therapy in patients with ovarian cancer. The healthier phase II patients did not receive as much benefit from the therapy, and the therapy was found to be cleared by their systems fairly quickly. To remedy the situation, we have designed and made a virus that has human proteins on the outside. This will help the virus survive longer while in the patient because it will not be seen as something 'foreign'. Patients will be treated with intra-abdominal infusions of a viral vector containing the full length BRCA1 gene in an attempt to stop the spread of the cancer and possibly induce regression. The patient population will consist of women with ovarian cancer who have completed standard initial surgery and chemotherapy and have either small amounts of residual cancer or have been found to have an early recurrence of their cancer.